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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,671	10/28/2003	Robert D. Ivarie	021396-000203US	6850

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EXAMINER
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KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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11/15/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

Application No.

10/696,671

Applicant(s)

IVARIE ET AL.

Examiner

Sumesh Kaushal

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 20,21,28-35,37,41,46,52-56 and 59-64 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20,21,28-35,37,41,46,52-56 and 59-64 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

*Claims 20-21, 28-35, 37, 41, 46, 52-56, 59-64 are pending and are examined in this office action.*

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **571-273-8300**.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Applicant's response and Dr. Ivarie' declaration filed on 08/15/07 has been acknowledged and fully considered.

***Claim Rejections - 35 USC § 112***

Claims 20-21, 28-35, 37, 41, 46, 52-56 and 59-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reason of record as set forth in the office action mailed on 10/30/07.

**Response to Argument and Dr. Ivarie's declaration (written description)**

The applicant argues that the application provides details of how to practice in a predictable and workable method for producing germ-line transgenic avian. The applicant argues that these germline transgenic avian have the phenotype of producing specific exogenous proteins in their oviduct and laying eggs containing the exogenous proteins. The applicant argues that as stated by Dr. Ivarie, the germline transgenic G1 birds were produced from the GO [ $\beta$ -lactamase birds using standard breeding methodologies apparent to practitioners of skill in the art, i.e., GO roosters containing transgene in their sperm were crossed with non-transgenic chickens. the applicant argues that numerous examples of specific proteins are provided in the specification which can be produced in accordance with the present invention, the coding sequences of which were well known in the art prior to the filing of the application. The applicant continues that in view of the declaration filed a practitioner of ordinary skill in the art would be able to make lines of germline transgenic avians that lay eggs containing many different proteins. The applicant argues that applicant has shown that the application as filed presented sufficient written description to enable members of the public to understand and carry out the invention producing a variety of exogenous proteins, which encompasses any transgenic avian (across class avis). In view of the Dr. Ivarie's declaration the applicant argues that since the infectivity of the ALV is not limited to chickens, production of birds other than chickens that lays eggs containing exogenous protein is within the reach of one skilled in the art according to the specification as filed

However the applicant's arguments are found not persuasive because the scope of transgenic avian, which lay eggs containing an exogenous protein of interest encompasses any transgenic avian (across class avis) which lays eggs containing any exogenous protein of interest. As stated earlier few disclosed embodiments are not representative of the products claimed. At best the specification as filed discloses the making of chimeric chickens by transducing stage X embryos with NLB-CMV-BL (ALV-based vector) transduction particles (spec page 32, example-3, page 33 lines 3-9). Even though the specification as filed teaches the production of  $\beta$ -lactamase in egg

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white the specification fails to disclose any germ line transgenic avian (even a chicken) whose egg contains any exogenous protein produced (to be purified) by any transgene (which is not limited to a particular structure) present in the germ line of the transgenic avian and wherein the exogenous protein is produced in the transgenic oviduct.

On the other hand at very best the Dr. Ivarie's declaration discloses transgenic chickens which are capable of producing the IFN $\alpha$ 2, EPO and G-CSF in the egg-white, using NLB-CMV-based vector system which randomly intergrated in the oviduct cells that produces egg-white. The declaration states that the use of the non-tissue specific CMV promoter to express the exogenous protein in the avian oviduct has been routine and has not required undue experimentation. The declaration further states that random integration of the NLB vector into the avian genome has not made practicing the invention unpredictable and has not imposed undue experimentation in order to practice the invention.

However the applicant's arguments are found not persuasive because in analyzing whether the written description requirement is met for the claimed invention, it is first determined whether a claimed genus (transgenic avian) have been described through sufficient description of a representative number of species by their complete structure and function. Although, it is not realistic to expect that the "complete structure" of an animal, or even a cell, could be described, the phenotype a transgenic animal with desired traits remains unpredictable phenomenon because it is the result of a complex interaction between animal genetics and environment. Therefore, the inquiry required by this portion of the written description guidelines is interpreted to be whether the phenotypic consequences of altering the genotype have been described.

Therefore, the limited disclosure in the specification (*which fails to produce even a single transgenic chicken*) is not deemed sufficient even in view of Dr. Ivarie's declaration (*that teaches only transgenic chickens encoding IFN $\alpha$ 2, EPO and G-CSF in the egg-white*) to reasonably convey to one skilled in the art that the applicants were in possession of the huge genera recited in the claims at the time the application was filed. Furthermore, It is noted that patent protection is granted in return for an enabling

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disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), *Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Thus it is concluded that the written description requirement is not satisfied for the claimed genera.

Claims 20-21, 28-35, 37, 41, 46, 52-56, 59-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a germ-line transgenic chicken which lays an egg containing an exogenous protein encoded by a transgene selected from group consisting of NLB-CMV-IFN $\alpha$ 2, NLB-CMV-EPO and NLB-CMV-G-CSF present in the germ-line of the transgenic chicken wherein the exogenous protein is produced in the transgenic chicken's oviduct and is deposited in the egg-while of the eggs produced, does not reasonably provide enablement for any other germline transgenic avian that lays eggs containing any exogenous protein encoded by a transgene present in the germline of the transgenic avian. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reason of record as set forth in the office action mailed on 10/30/07.

**Response to Argument and Dr. Ivarie's declaration (enablement)**

The applicant argues that in view of Ivarie Declaration, which teaches germline transgenic chickens that lay eggs containing EPO, G-CSF and interferon alpha 2, it is understood by a practitioner of ordinary skill in the art would be able to make and use the invention as claimed without undue amount of experimentation which encompasses making and use of any germ line transgenic avian that lays eggs containing any

exogenous protein encoded by a transgene present in the germline of the transgenic avian.

However the applicant's arguments are found not persuasive because the scope of transgenic avian, which lay eggs containing an exogenous protein of interest encompasses any transgenic avian (across class avis) which lays eggs containing any exogenous protein of interest. At best the specification as filed discloses the making of chimeric chickens by transducing stage X embryos with NLB-CMV-BL (ALV-based vector) transduction particles (spec page 32, example-3, page 33 lines 3-9). Even though the specification as filed teaches the production of b-lactamase in egg white the specification fails to disclose any germ line transgenic avian (even a chicken) whose egg contains any exogenous protein produced (to be purified) by any transgene (which is not limited to a particular structure) present in the germ line of the transgenic avian and wherein the exogenous protein is produced in the transgenic oviduct. On the other hand at very best the Dr. Ivarie's declaration discloses transgenic chickens which are capable of producing the IFN $\alpha$ 2, EPO and G-CSF in the egg-white, using NLB-CMV-based vector system which randomly intergrated in the oviduct cells that produces egg-white.

Since the specification fails to disclose the making of any other germ line transgenic avian whose egg contains any exogenous protein produced (to be purified) by transgene present in the germ line of the transgenic avian and wherein the exogenous protein is produced in the transgenic oviduct, it is unclear how one skilled in the art use the invention as claimed (supra). The applicant's disclosure does not enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation, which requires making any avian species which is germ line transgenic avian whose egg contains any exogenous protein produced by any transgene present in the germ line of the transgenic avian and wherein the exogenous protein is produced in the transgenic oviduct.

At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be

expected of one of ordinary skill in the art." See *Fields v. Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). In instant case making a germ line transgenic avian capable of producing eggs that contains an exogenous protein of interest by using any transgene construct (which is not oviduct tissue specific) is not considered routine in the art and without sufficient guidance to a germ line specific transgenic avian species, transgene construct and the production of the encoded product in the egg white the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). The state of the art at the time of filing regarding making germ-line transgenic birds that produces an exogenous protein of interest in the eggs is considered highly unpredictable especially in view of low transgene transmission to the progeny.

In addition viral the integration of viral vectors in the genome is random which further renders the any tissue specific (i.e. oviduct) highly unpredictable even in the presence of tissue specific promoter (Sang Mechanisms of Development 121:1179-1186, 2004, see pages 1182-1184; Mozdziak et al, Developmental Dynamics 229:414-421, 2004, see pages 416-418). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

### ***Double Patenting***

Claims 20-21, 28-35, 37, 41, 46, 52-56 and 59-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 11/337,302, for the reason of record as set forth in the office action mailed on 10/30/07.



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Claims 20-21, 28-35, 37, 41, 46, 52-56 and 59-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 11/274,674, for the reason of record as set forth in the office action mailed on 10/30/07..

Claims 20-21, 28-35, 37, 41, 46, 52-56 and 59-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 11/100,255, for the reason of record as set forth in the office action mailed on 10/30/07.

Claims 20-21, 28-35, 37, 41, 46, 52-56 and 59-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 11/099,934, for the reason of record as set forth in the office action mailed on 10/30/07.

Claims 59-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 11/337,361, for the reason of record as set forth in the office action mailed on 05/15/07, for the reason of record as set forth in the office action mailed on 10/30/07.

Claims 20-21, 28-35, 37, 41, 46, 52-56 and 59-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 of copending Application No. 11/376,023, for the reason of record as set forth in the office action mailed on 10/30/07.

**Response to Argument (double patenting)**

The applicant argues that should any one of the cited co-pending applications issue before the allowance of the present application, applicant is willing to consider the possibility of filing an appropriate terminal disclaimer. Therefore the rejections above has been maintained.

**Conclusion**

No claims are allowed.

This is a RCE of applicant's earlier Application No. 10696671. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
**SUMESH KAUSHAL**  
**PRIMARY EXAMINER**